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08/487,032	06/07/1995	DOUGLAS SMITH	GTN-001	7279

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	20

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/487,032	SMITH, DOUGLAS	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *28 May 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *123,132,133,149,202,203,212 and 220-235* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *123,132,133,149,202,203,212 and 220-235* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 202-203, 212, 220-224 have been amended; new claims 225-235 have been added.
2. Claims 123, 132, 133 and 149 depend from the amended claims.
3. Claims 123, 132, 133, 149, 202-203, 212, and 220-235 are pending.
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections/Objections Withdrawn

5. The claims are no longer rejected under 35 USC 101, lack of utility in light of the fact that the polypeptide, encoded by SEQ ID NO 809, is a bacterial pathogen polypeptide that comprises a T-cell epitope.

6. The pending claims rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, in light of the lack of utility rejection having been withdrawn herein.

7. Claims 123,132 and 202-203 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is herein withdrawn in light of Applicant traversal.

Rejections Maintained

8. The Specification, the original Drawings and the sequence pages do not correspond to one another for reasons of record (see paper number 42, paragraph 6 and 7) and drawing and Specification objections set forth below. Figures 559 and 560 have been deleted.

9. Claims 123, 132-133, 149, 202-203, 212 and 220-224 and new claims 225-235 rejected under 35 U.S.C. 112, first paragraph (written description), as failing to comply with the written

description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Response to Amendment

10. Applicant requested the reconsideration of the Declaration of Dr. Peter C. Doig filed March 4, 2002 under 37 CFR 1.132 in light of the submission of the newly amended claims, and new claims added in response to the Non-Final Office Action dated April 30, 2002.

11. Upon reconsideration of the Declaration of Dr. Peter C. Doig, it was noted that Dr. Doig's signature was shown at page 4, of the Declaration but was not dated, and the typed line shows March 1, 2002, without Dr. Doig filling in the date. The Declaration appears to not be fully executed.

12. Additionally, with respect to the rejections set forth under 35 USC 101, and 112, first paragraph (enablement based upon a lack of utility), the examiner would like to point out the fact that these rejections have been herein withdrawn. The Declaration will be reconsidered by the examiner in so far as the Declaration applies to the outstanding rejection under 35 USC 112, first paragraph (lack of written description) over the claimed genus of polypeptides that comprise a conserved T-cell epitope.

13. Dr. Doig et al states on page 2, paragraph (A) that HopE is a 239 amino acid polypeptide.

14. Based upon the evidence provided by Dr. Doig's Declaration, it can be ascertained that SEQ ID NO 809 is an incomplete amino acid sequence encoded by an incomplete open reading

frame for an Helicobacter pylori polypeptide. The instant specification does not describe SEQ ID NO 809 to be embedded within another amino acid sequence, to be contained in a larger polypeptide, nor to originate from HopE, wherein SEQ ID NO 809 sets forth 148 amino acids, not 239 amino acids.

15. Dr. Doig et al states that HopE is identical to SEQ Id NO 764 (which is now SEQ ID NO 809) at "amino acid residues 24 through 155".

16. It is the position of the examiner that SEQ ID No 809 only has 148 amino acid residues, and not 155 as asserted by Dr. Doig. The reference sequence to which Dr. Doig refers does not evidence original descriptive support in the instant Specification.

17. Dr. Doig, at paragraphs (B and C) pages 2-3 of the Declaration, states that epitope mapping was accomplished utilizing overlapping peptides of 10-mers, and found epitopes to be represented in SEQ ID NO 764 (see Table 1).

18. It is the position of the examiner that the epitopes shown in Table 1 represented by the species sequences shown in the Table and not specifically disclosed in the instant specification. While the entire polypeptide contains these sequences, the epitope sequences of 10 amino acids discussed by Dr. Doig, do not evidence original descriptive support in the instant specification. No specific sub fragments of SEQ ID NO 809 are disclosed in the instant specification, and evidence original descriptive support. The claims are not directed to a polypeptide that "consists of SEQ ID No 809", but is directed to a genus of polypeptides, obtained from any source, and are of any over all sequence, with no specified biological activity (such as enzymatic activity), but

must comprise any sequence of at least 10 consecutive amino acids of SEQ Id NO 809, and which can be recognized by a T-cell receptor. Dr. Doig's evidence does not define a genus of polypeptides that comprise the specific amino acid sequence identified by his experiments. What is claimed is a polypeptide that comprises any 10 consecutive amino acids of SEQ Id NO 9, and comprise a T-cell receptor epitope.

The examiner would like to cite Amara et al (Feb. 1995) to show that methionine, "Met", can be immunogenic, antigenic, and interact with a T-cell epitope, upon being conjugated to a carrier, for the induction of antibodies. Therefore, the claims read on, in light of the teachings of the prior art, any sequence of amino acids that comprises "Met" methionine and contains 10 consecutive amino acid of SEQ Id NO 809. The specification does not provide original descriptive support for the genus of polypeptides now claimed based upon disclosure of a single species of polypeptide represented by SEQ ID NO 809; Seq ID NO 809 not being the complete amino acid for HopE of Helicobacter pylori, as discussed by Dr. Doig.

Additionally, the instant Specification proposes to identify epitopes contained in the disclosed polypeptides through suggesting at page 60, paragraph 4 "immunogenic H.pylori fragments can be identified by the ability of the peptide to stimulate T-cells". Suggesting the identification of epitope containing peptides, does not show possession of a genus of peptides that comprise a conserved epitope that has yet to be identified. It is also noted that the polypeptides of 202-203,212,221-228,230-235 are not limited to H.pylori polypeptides.

19. Dr. Doig concludes his Declaration with the statement that "the claimed polypeptides, including those shown in Table 1 above, have the ability to induce an immune response".

20. It is the position of the examiner that the claimed genus of polypeptides have not been described by a represented number of species, and the structure of the polypeptides have not been so claimed based upon a defined structure correlated with a specific biological function (enzymatic activity, or immunoreactivity that is diagnostic of disease or induces a therapeutic immune response). For the reasons cited above, and set forth by the examiner in the rejection under 35 USC 112, first paragraph (written description) made of record previously, the Declaration of Dr. Doig, which was produced after the filing date of the instant Specification, is insufficient to obviate the rejection of the claims under 35 USC 112, first paragraph (written description) showing possession of what is now claimed, at the time of filing.

21. The rejection of claims 123, 132-133, 149, 202-203, 212 and 220-224 and new claims 225-235 under 35 U.S.C. 112, first paragraph (written description), as failing to comply with the written description requirement, wherein the claims are directed to subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is traversed on the grounds that:

a. "the polypeptides of claims 202 and 203 are limited to those polypeptides which have the same identifying characteristics, e.g. functional and structural characteristics"

22. It is the position of the examiner that all of the claims are directed to polypeptides that comprise a antigenic, immunogenic or T-cell receptor fragment encoded by SEQ ID NO 809, but no epitopes of 10, 12, 16 or 20 amino acid sequences evidence original descriptive support. No polypeptides that comprise additional amino acids to the 148 amino acids represented in SEQ ID

NO 809 have been disclosed, nor evidence original descriptive support in the instant Specification.

23. Each claim is directed to genus of polypeptides that share an amino acid sequence of SEQ ID NO 809, but only a single species is disclosed and SEQ ID NO 809 is not representative of a highly variable genus of polypeptides that may comprise any number of amino acids, and evidence any type of biological function, as long as there is amino acid sequence held in common, the amino acid sequence being recognized by a T-cell receptor. No T-cell receptor recognition amino acid sequences other than SEQ ID NO 809 has been disclosed, and the specification proposes to identity additional sequences in the future (see instant specification page 60). The lack of written description is over the scope of what is now claimed, in light of the genus of polypeptides having not been described by structure correlated by function, the structure held in common, not having been described, other than the entire sequence of SEQ ID NO 809.

24. Polypeptides which are much larger than SEQ ID NO 809 are encompassed by the claims. No polypeptides larger than SEQ Id No 809 evidence original descriptive support. HopE, is a porin polypeptide of over 200 amino acids; this protein/polypeptide has not been described in the instant specification.

25. The specification invites the person of skill in the art to do additional experimentation (instant Specification, page 60); this does not show possession of the claimed genus of polypeptides set forth in the claims. The lack of written description rejection under 35 USC 112, first paragraph is maintained for reasons of record; a single species does not describe a highly variable genus of polypeptides.

New Grounds of Objection and Rejection Necessitated by Amendment

SEQUENCE LISTING

26. The sequence listing submitted on CD Rom does not correspond identically to the originally filed Figures/sequences; Figures 559 and 560 have been deleted from the Brief Description of the Drawings.

Drawings

27. New corrected drawings are required in this application because all of the sequence identifiers have been changed relative to figures submitted, for the following reasons:

b. Figures 559 and 560 have been completely deleted from the Specification; this is new matter.

c. Original figure notations have been changed, for example original Figure 426A, was referred to as:

28. "SEQ ID NO 38080063_c2_9:AA" , page 509, Figure 426A, polypeptide HPP426, and SEQ ID NO 764, but now

(a) Figure 426A, polypeptide (426A), and SEQ ID NO 509.

d. Page 6, paragraph 4, of the Specification refers to Figure 559 which has been deleted, but the narrative at this location has not been modified.

e. No Figure showing the polypeptide referred to as HPP426A has been submitted, and the Specification at page 39, mentions HPP426 polypeptide; two different terms are being used and not defined to be one and the same polypeptide.

f. Page 57 paragraph 1 refers to Figures 1A -*B; there are not figures labeled *B.

g. Page 63, paragraph 2, refers to Figure 560, which has been deleted by Applicant's Amendment.

h. Page 72, paragraph 3 refers to Figure 559 which has been deleted.

29. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

30. The disclosure is objected to because of the following informalities: The Specification is objected to as the Brief Description of the Drawings and references to the Drawings made through out the original Specification do not correspond to the Brief Description of the Drawings submitted by Applicant's Amendment dated November 12, 2002. The Specification refers to Drawings that no longer evidence description in the Brief Description of the Drawings and the Drawings have been completely deleted from the Specification, ie Figure 560 and 559. Appropriate correction is required.

Claim Rejections - 35 USC § 112

31. Claims 232 and 233 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 232 and 233 recite the phrase "no more than 148 amino acid residues of SEQ ID NO:809". This phrase appears to define SEQ ID NO 809 to be representative of more than 148 amino acids; this is confusing in light of the fact that SEQ ID NO 809 represents only 148 amino

acids and the claimed polypeptide can be or comprises a polypeptide larger than 148 amino acids. The invention is not clearly set forth.

Claim Rejections - 35 USC § 102

32. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> i. A person shall be entitled to a patent unless –
>
> j. the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> k. the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

33. Amended Claims 123,132-133,149, 202-203, 212,220-224, and New Claims 225-235 are rejected under 35 U.S.C. 102(a) as being anticipated by Doig et al (Infection and Immunity, October 1994, reference of record in paper number 32), based upon the evidence provided by Doig et al (October 1995, reference of record), the complete HopE amino acid sequence of Swiss-Prot Q9ZLD5, and Applicant's Declaration provided by Dr. Doig et al, submitted under 37 CFR 1.132.

34. Doig et al (1994) disclose the instantly claimed invention directed to:

an isolated polypeptide (31, 50 and 90 kDa polypeptides, see page 4531,col 2) that comprises at least one epitope recognized by a T-cell receptor (see Doig et al, 1994, table 1, page 4528, the polypeptides were found to be immunoreactive with monoclonal antibodics(see Doig et al, (1994). page 4531, column 2, last paragraph and page 4528, top of page, monoclonal antibodies listed in Table), thus disclosing the polypeptides that are:

(New Instant claim 225) recognized by a T-cell receptor (see Doig et al, 1994);

(New Instant claim 226) to comprise at least one antigenic determinant;

(Amended and **New Instant claims 123, 227**) the claimed product by process polypeptide of claims 123 and 227, do not evidence any structural differences between the native polypeptide and the claimed recombinant polypeptide, the native polypeptide of the prior art anticipates the instant claimed polypeptides produced by the process step defined by the recitation of the term "recombinant" (it was noted that the nucleic acid that encodes the amino acid sequence of SEQ ID NO 809 is not included in the Brief Description of the Drawings;

(Amended and **New Instant claims 133, 228-229**) an H.pylori polypeptide that comprises at least 10, 12, 16, 50 and 100 amino acids of SEQ ID NO 809 and an additional amino acid sequence, wherein SEQ ID NO 809 consists of 148 amino acids and the proteins of Doig et al (1994) comprised more than 148 amino acids, about 270 amino acids. The polypeptide of Doig et al (1994) comprised at least 10 consecutive amino acids of SEQ Id No 809 and an additional amino acid sequence (see Swiss-Prot amino acid sequence alignment of HopE, and the sequence of Doig et al (1995) and the inherent amino acid sequence of the polypeptide of Doig et al 1994).

(Amended and New **Instant claims 149, 230, 231**) a pharmaceutically acceptable carrier (see page 4527, col. 2, paragraph 3, "Milli Q water" was combined with the isolated and purified polypeptides of Doig et al (1994).

(New **Instant claims 232-235**) The polypeptide of Doig et al (1994) did not comprise all 148 amino acid sequence of SEQ ID No 809, as the sequence of Doig et al (1995) shows a difference from SEQ ID NO 809, by an amino acid "X" (see top of page 5450, col. 1, Figure 5, third amino acid from the end of HopE sequence); and the Swiss Prot amino acid sequence provide evidence that the polypeptides of Doig et al (1994 and

1995) did not to comprise the amino acids "Glu Ile Ile" of SEQ ID NO 809) thus the polypeptide of Doig et al (1994) does not comprise "more than 148 amino acid residues of SEQ ID NO 809, based upon the evidence provided by Doig et al (1995) and the complete HopE amino acid sequence of Swiss-Prot Q9ZLD5. The polypeptides of Doig et al (1994) comprised at least 10 consecutive amino acid residues of SEQ ID NO 809 which encodes an antigenic determinant, as well as encodes an epitope, as the polypeptides of Doig et al (1994) induced an immune response (epitope) and immunoreacted (antigenic determinant) with monoclonal antibodies produced thereto.

35. Amended Claims 123,132-133,149, 202-203, 212,220-224, and New Claims 225-235 are rejected under 35 U.S.C. 102(b) as being anticipated by Tufanao et al (April 1994, reference of record) as evidenced by the complete HopE amino acid sequence of Swiss-Prot Q9ZLD5, and Applicant's Declaration provided by Dr. Doig et al, submitted under 37 CFR 1.132.

Tufanao et al disclose the instantly claimed invention directed to an isolated polypeptide of Helicobacter pylori, wherein the polypeptide comprises an epitope that will react with a T-cell receptor and is a porin of about 30 kDa and referred to by the Declaration submitted by Applicant, by Dr. Doig to be HopE, a 30 Kda H.pylori porin polypeptide. The porin polypeptide of Tufanao et al comprised a T-cell receptor binding epitope (see Tufanao et al, title and entire reference that shows cytokine stimulation and production by human white blood cells, see all Tables; and page 1397, bottom of column 1, and first paragraph of column 2), and stimulated an immune response.

The purified porin polypeptide of about 30 kDa was isolated and combined with SDS buffer in 0.1M sodium phosphate [pH 7.2] , an acceptable carrier, and was further enriched followed by dialysis (see page 1393, col. 1, lines 1-5, first paragraph).

Inherently the porin polypeptide of Tufanao et al comprises an amino acid sequence of SEQ ID NO 809 in light of the evidence provided by the amino acid sequence for HopE porin, an about 30 kDa polypeptide of H.pylori (Swiss-Prot amino acid Accession Number:Q9zld5) and the Declaration of Dr. Doig which teaches SEQ ID NO 764, which is now SEQ ID NO 809, to be a HopE polypeptide, a polypeptide of about 30 kDa and functions as an Helicobacter pylori porin.

The amino acid sequence of the porin of Tufanao et al is an inherent structural characteristic. See Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. "The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art".

Conclusion

36. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Vgp
April 29, 2004

L. F. Smith

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